UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: February 2, 2015

SUBJECT: Glufosinate-Ammonium: Agency's Review of Bayer CropScience's submission "Examination on the Refined Analysis of Mean Length of the Ventral Limb of the Dentate Hilus from Postnatal Day 72 rats in a Developmental Neurotoxicity Study."

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CONCLUSION: Health Effects Division (HED) reviewed the data submitted by the Registrant and reiterates its earlier conclusion that the morphometric changes observed at the the lowest dose tested in the developmental neurotoxicity study are treatment related and that a No Observed Adverse Effect Level (NOAEL) was not established in the offspring in that study.

I. ACTION REQUESTED

Bayer CropScience has submitted a re-evaluation of morphometric findings in a previous developmental neurotoxicity study (MRID 46455701). This memo responds to the re-evaluation of the morphometric findings.

II. BACKGROUND

In 2005, HED reviewed a developmental neurotoxicity (DNT) study (MRID 46455701) with glufosinate-ammonium; HED determined that there was a dose-dependent decrease in the length of the ventral limb of the dentate hilus (brain morphometric measurement) in PND72 males and females at all dose levels. Based on these results, HED identified an offspring LOAEL of 200 ppm (14 mg/kg/day); a NOAEL was not observed (TXR# 0053106).

In response to this review, the Registrant (Bayer CropScience) requested the test laboratory (WIL Research) to verify the suitability of the sections used for morphometric analysis and "cursor" placement for the particular measure of length of the ventral limb of the dentate hilus. Consequently, a review was performed by a panel of 3 individuals (two pathologists and a technician).

For the review, images were re-evaluated for section quality, level, homology, and uniform cursor placement. Based on this review, Bayer concluded that glufosinate-ammonium is associated with significantly lower group mean ventral limb of the dentate hilus in the high-dose males (4500 ppm or 292 mg/kg/day). There were no statistically significant effects at the low (200 ppm or 14 mg/kg/day)- or mid-doses (1000 ppm or 69 mg/kg/day) for males, or in females at any dose level (MRID No.: 49331201 - 203).

III. HED Review of the Submission

Following the review of the submitted data, HED has concerns about the poor quality of sections and the lack of reliable and accurate brain morphometric measurements. Several measurements were excluded because of poor section quality (which was acknowledged by Bayer). There is also concern regarding WIL laboratories experience with the particular morphormetric measurement of the length of the dentate hilus which they acknowledge is an "uncommon measure of the hippocampus", and in their experience is "more variable than all other brain morphometry measures." In addition, HED notes that comparison of the group means for control male and female rats in Bayer's refined analysis is limited by the refinement of the cursor placement relative to that used for the historical control studies, rendering the data difficult to interpret. Based on these concerns, HED concludes that there is uncertainty because of the lack of a full set of appropriate brain morphometric data. Consequently, HED

reiterates that the brain morphometric changes observed at the low dose are treatment related and a NOAEL was not established for the offspring in this study.